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LOGINID:ssspta1623zct

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 01	INPADOC: New family current-awareness alert (SDI) available
NEWS	4	SEP 01	New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS	5	SEP 01	New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
NEWS	6	SEP 27	STANDARDS will no longer be available on STN
NEWS	7	SEP 27	SWETSCAN will no longer be available on STN
NEWS	8	OCT 28	KOREAPAT now available on STN
NEWS	9	NOV 18	Current-awareness alerts, saved answer sets, and current search transcripts to be affected by CERAB, COMPUAB, ELCOM, and SOLIDSTATE reloads
NEWS	10	NOV 30	PHAR reloaded with additional data
NEWS	11	DEC 01	LISA now available on STN

NEWS EXPRESS		OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS		STN Operating Hours Plus Help Desk Availability
NEWS INTER		General Internet Information
NEWS LOGIN		Welcome Banner and News Items
NEWS PHONE		Direct Dial and Telecommunication Network Access to STN
NEWS WWW		CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 07:19:11 ON 02 DEC 2004

=> FILE REG

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 07:19:14 ON 02 DEC 2004
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STRUCTURE FILE UPDATES: 30 NOV 2004 HIGHEST RN 791034-84-9
DICTIONARY FILE UPDATES: 30 NOV 2004 HIGHEST RN 791034-84-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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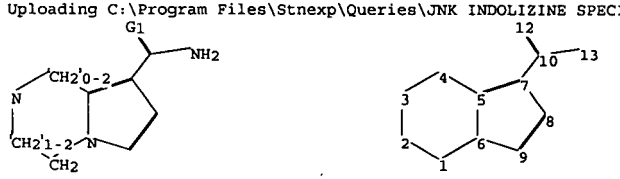
Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\JNK INDOLIZINE SPECIAL.str



chain nodes :
10 12 13
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
7-10 10-12 10-13
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9
exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 10-12 10-13
exact bonds :
7-10

G1:O,S

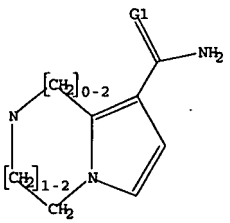
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
12:CLASS 13:CLASS

L1 STRUCTURE UPLOADED

=> D L1
L1 HAS NO ANSWERS
L1 STR

STN SEARCH TRANSCRIPT

10/803,566



G1 O,S

Structure attributes must be viewed using STN Express query preparation.

=> S L1
SAMPLE SEARCH INITIATED 07:19:30 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 208 TO ITERATE

100.0% PROCESSED 208 ITERATIONS 16 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 3295 TO 5025
PROJECTED ANSWERS: 80 TO 560

L2 16 SEA SSS SAM L1

=> FILE CAPLUS
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.42 0.63

FILE 'CAPLUS' ENTERED AT 07:19:37 ON 02 DEC 2004
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FILE COVERS 1907 - 2 Dec 2004 VOL 141 ISS 23
FILE LAST UPDATED: 1 Dec 2004 (20041201/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L2
L3 1 L2

=> D

L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:242334 CAPLUS
DN 138:255255
TI Preparation of 1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazine-8-carboxamides as protein kinase inhibitors for treatment of cancer
IN Ratcliffe, Andrew James; Walsh, Rodger John Aitchison; Majid, Tahir Nadeem; Thurairatnam, Sukanthini; Amendola, Shelly; Aldous, David John; Souness, John Edward; Nemecek, Conception; Wentzler, Sylvie; Venot, Corinne
PA Aventis Pharma S.A., Fr.
SO PCT Int. Appl., 269 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003024967	A2	20030327	WO 2002-EP11131	20020917
	WO 2003024967	A3	20030904		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1436291	A2	20040714	EP 2002-772360	20020917
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	GB 2001-22560	A	20010919		
	US 2002-355860P	P	20020211		
	WO 2002-EP11131	W	20020917		

OS MARPAT 138:255255

APPLICANTS

PRIORITY APP'N.

=> FILE REG
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 1.50 2.13

FILE 'REGISTRY' ENTERED AT 07:20:08 ON 02 DEC 2004
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STRUCTURE FILE UPDATES: 30 NOV 2004 HIGHEST RN 791034-84-9
DICTIONARY FILE UPDATES: 30 NOV 2004 HIGHEST RN 791034-84-9

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more

information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> S L1 SSS FULL
FULL SEARCH INITIATED 07:20:13 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 4398 TO ITERATE

100.0% PROCESSED 4398 ITERATIONS 307 ANSWERS
SEARCH TIME: 00.00.01

L4 307 SEA SSS FUL L1

=> FILE CAPLUS

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	155.42	157.55

FILE 'CAPLUS' ENTERED AT 07:20:19 ON 02 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 2 Dec 2004 VOL 141 ISS 23
FILE LAST UPDATED: 1 Dec 2004 (20041201/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> S L4
L5 3 L4

=> S L5 NOT L3
L6 2 L5 NOT L3

=> D 1-2 IBIB ABS HITSTREW
'HITSTREW' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
SCAN must be entered on the same line as the DISPLAY,
e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, IPC, and NCL

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field
codes. For a list of the display field codes, enter HELP DFIELDS at
an arrow prompt (=>). Examples of formats include: TI; TI,AU; BIB,ST;
TI,IND; TI,SO. You may specify the format fields in any order and the
information will be displayed in the same order as the format
specification.

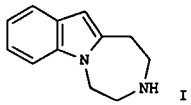
All of the formats (except for SAM, SCAN, HIT, HITIND, HITRN, HITSTR,
FHITSTR, HITSEQ, FHITSEQ, KWIC, and OCC) may be used with DISPLAY ACC
to view a specified Accession Number.
ENTER DISPLAY FORMAT (BIB):END

=> D 1-2 IBIB ABS HITSTR

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2003:485892 CAPLUS
DOCUMENT NUMBER:	139:245990
TITLE:	2,3,4,5-Tetrahydro- and 2,3,4,5,11,11a-hexahydro-1H-[1,4]diazepino[1,7-a]indoles: new templates for 5-HT2C agonists
AUTHOR(S):	Ennis, Michael D.; Hoffman, Robert L.; Ghazal, Nabil B.; Olson, Rebecca M.; Knauer, Christopher S.; Chio, Chris L.; Hyslop, Deborah K.; Campbell, Jeffery E.; Fitzgerald, Lawrence W.; Nichols, Nanette F.; Svensson, Kjell A.; McCall, Robert B.; Haber, Christopher L.; Kagey, Michelle L.; Dinh, Dac M.
CORPORATE SOURCE:	Medicinal Chemistry III, Pharmacia Corporation, Kalamazoo, MI, 49009, USA
SOURCE:	Bioorganic & Medicinal Chemistry Letters (2003), 13(14), 2369-2372 CODEN: BMCLE8; ISSN: 0960-894X

PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:245990
GI

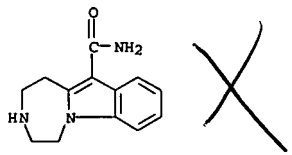


I

AB The design and synthesis of the novel 2,3,4,5-tetrahydro-1H-[1,4]diazepino[1,7-a]indole (I) is described. This azepinoindole has excellent affinity for 5-HT2C (Ki 4.8 nM) and modest selectivity over 5-HT2A (.apprx.4-fold). Several N- and C11-substituted analogs of 5 were prepared, as were a number of biaryl indoline derivs. The anxiolytic potential for the azepinoindole template I is demonstrated by activity in a mouse shock-aggression assay.

IT **364344-84-3**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(affinity for 5-HT2C agonist)

RN 364344-84-3 CAPLUS
CN 1H-[1,4]Diazepino[1,7-a]indole-11-carboxamide, 2,3,4,5-tetrahydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:730745 CAPLUS
DOCUMENT NUMBER: 135:288799
TITLE: Preparation of 2,3,4,5-tetrahydro-1H-[1,4]diazepino[1,7-a]indoles as 5-HT receptor antagonists for treatment of CNS disorders
INVENTOR(S): Ennis, Michael Dalton; Hoffman, Robert Louis; Ghazal, Nabil B.; Olson, Rebecca M.
PATENT ASSIGNEE(S): Pharmacia & Upjohn Co., USA
SOURCE: PCT Int. Appl., 331 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

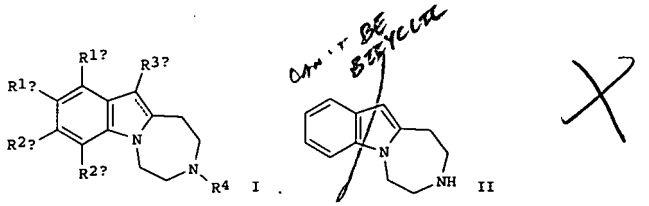
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001072752	A2	20011004	WO 2001-US4950	20010308
WO 2001072752	A3	20030417		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2402472	AA	20011004	CA 2001-2402472	20010308
AU 2001043163	A5	20011008	AU 2001-43163	20010308
US 2002002161	A1	20020103	US 2001-803242	20010308
US 6734301	B2	20040511		
EP 1328525	A2	20030723	EP 2001-916099	20010308
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003529569	T2	20031007	JP 2001-570662	20010308
ZA 2002007341	A	20040121	ZA 2002-7341	20020912
US 2004209870	A1	20041021	US 2004-761070	20040120
PRIORITY APPLN. INFO.:			US 2000-189103P	P 20000314
			US 2001-803242	A3 20010308
			WO 2001-US4950	W 20010308

OTHER SOURCE(S): MARPAT 135:288799
GI



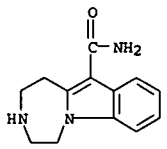
I II

AB Title compds. I [wherein R1a, R1b, R2a, and R2b = independently (a) H, halo, CN, CF3, OCF3, OR5, CONR5R6, COR5, CO2R5, Y(CH2)mXR5, YCO(CH2)mXR5; m = 0-3; Y = CH2, S, O, or NR6; X = CH2, S, O, NR6; (b) (CH2)pAr; p = 0-3; Ar = (un)substituted (hetero)aryl or (c) (un)substituted (cyclo)alkyl, (cyclo)alkenyl, or (cyclo)alkynyl; R3 = (a) H, halo, CN, CF3, OCF3, alkyl, Ar, OR5, SR5, CHO, CONR5R6, COR5, CO2R5, Yo(CH2)nXR5, COCONXR5, Yo(CH2)nN(R6)CONR5R6; o = 0 or 1; n = 0-3; X = CH, S, O, or NR6; Y = CH, S, O or NR6; Ar = (un)substituted (hetero)aryl; (b) (un)substituted (cyclo)alkyl, (cyclo)alkenyl, or (cyclo)alkynyl; R4, R5, and R6 = independently (a) H or (un)substituted (cyclo)alkyl, (cyclo)alkenyl, or (cyclo)alkynyl; (b) (CH2)pAr; p = 0-3; Ar = (un)substituted (hetero)aryl; or stereoisomers or pharmaceutically acceptable salts thereof] were prepared For example, 2,3,4,5-tetrahydro-1H-[1,4]diazepino[1,7-a]indole•HCl (II•HCl) was prepared in a multi-step synthesis starting from Et H malonate and 2-nitrophenylacetic acid and involving the cyclization of the Et [1-(2-bromoethyl)-2,3-dihydro-1H-indol-2-yl]acetate intermediate to the tetrahydro-1H-[1,4]diazepino[1,7]indol-2(3H)-one. I are useful as 5-HT receptor antagonists for the treatment of a variety of central nervous system disorders (no data).

IT **364344-84-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1H-[1,4]diazepino[1,7-a]indoles as 5-HT receptor inhibitors for treatment of CNS disorders)

RN 364344-84-3 CAPLUS
CN 1H-[1,4]Diazepino[1,7-a]indole-11-carboxamide, 2,3,4,5-tetrahydro- (9CI)

(CA INDEX NAME)



=> LOG HOLD
COST IN U.S. DOLLARS — SINCE FILE ENTRY: 10.84 — TOTAL SESSION: 168.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) — SINCE FILE ENTRY: -1.40 — TOTAL SESSION: -1.40

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 07:22:07 ON 02 DEC 2004

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1623zct

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 07:26:30 ON 02 DEC 2004
FILE 'CAPLUS' ENTERED AT 07:26:30 ON 02 DEC 2004
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COST IN U.S. DOLLARS — SINCE FILE ENTRY: 10.84 — TOTAL SESSION: 168.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) — SINCE FILE ENTRY: -1.40 — TOTAL SESSION: -1.40

=> FILE MEDLINE
COST IN U.S. DOLLARS — SINCE FILE ENTRY: 10.84 — TOTAL SESSION: 168.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) — SINCE FILE ENTRY: -1.40 — TOTAL SESSION: -1.40

FILE 'MEDLINE' ENTERED AT 07:26:37 ON 02 DEC 2004

FILE LAST UPDATED: 1 DEC 2004 (20041201/UP). FILE COVERS 1950 TO DATE.

On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD for details.

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> S JNK
          5977 JNK
           436 JNKS
L7        6059 JNK
               (JNK OR JNKS)

=> S L7 AND REVIEW
        380746 REVIEW
         47468 REVIEWS
        417972 REVIEW
                (REVIEW OR REVIEWS)
L8         132 L7 AND REVIEW

=> S L8 AND 2001/PY
        516039 2001/PY
L9          21 L8 AND 2001/PY

=> D 1-21 IBIB ABS
```

L9 ANSWER 1 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2002340255 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12082227
TITLE: The **JNK** and p38 signal transduction following axotomy.
AUTHOR: Herdegen T; Waetzig V
CORPORATE SOURCE: Institute of Pharmacology, University of Kiel, Hospitalstrasse 4, Germany.. t.herdegen@pharmakologie.uni-kiel.de
SOURCE: Restorative neurology and neuroscience, **(2001)** 19 (1-2) 29-39. Ref: 93
Journal code: 9005499. ISSN: 0922-6028.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020627
Last Updated on STN: 20020807
Entered Medline: 20020806

AB The transection of nerve fibers evokes a characteristic reaction in the injured neurons, the so-called cell body response (CBR), which comprises aspects of developmental re-differentiation with parallel loss of the transmittory phenotype, efforts or achievement of axonal elongation and re-construction of effective synapses. Neither the signals underlying the onset of CBR nor the programs underlying regeneration are sufficiently elucidated. Here we **review** the putative role of two subfamilies of the MAP kinases, the **JNKs** (c-Jun N-terminal kinases) and the p38 kinases in the CBR. Following nerve injury with subsequent CBR, **JNKs** are rapidly activated and this activation persists for weeks until neu-ronal cell death or successful regeneration. The various functions render **JNKs** to perfect candidate molecules for the realization of the CBR including axonal transport, activation of c-Jun,

modulation of cytoskeletal functions, detection of cytoskeletal alterations, or signal transduction of adhesion molecules in the axon and growth cone. On the other hand, the rapid but transient activation of p38 might interfere with the mitotic arrest, a putative feature of the CBR.

L9 ANSWER 2 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2002252929 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11991680
TITLE: Role of mitogen-activated protein kinases in the response of tumor cells to chemotherapy.
AUTHOR: Fan M; Chambers T C
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, University of Arkansas for Medical Sciences, Little Rock, AR 72205, USA.
CONTRACT NUMBER: CA75577 (NCI)
SOURCE: Drug resistance updates : reviews and commentaries in antimicrobial and anticancer chemotherapy, **(2001 Aug)** 4 (4) 253-67. Ref: 113
Journal code: 9815369. ISSN: 1368-7646.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020507
Last Updated on STN: 20020530
Entered Medline: 20020529

AB Antitumor agents, despite having diverse primary mechanisms of action, mediate their effects by inducing apoptosis in tumor cells. Cellular commitment to apoptosis, or the ability to evade apoptosis in response to damage, involves the integration of a complex network of survival and death pathways. Among the best-characterized pathways regulating cell survival and cell death are those mediated by the mitogen-activated protein kinase (MAPK) family. Not surprisingly, MAPK signaling pathways have been implicated in the response of tumor cells to chemotherapeutic drugs. Indeed, literature in this area has grown enormously in recent years, and the present **review** attempts to provide an overview and perspective of these advances. While the activities of the major MAPK subgroups are subject to modulation upon exposure of different types of cancer cell lines to diverse classes of antitumor agents, the response tend to be context-dependent, and can differ depending on the system and conditions. Despite these complexities, some important trends have surfaced, and molecular connections between MAPK signaling pathways and the apoptotic regulatory machinery are beginning to emerge. With increased evidence supporting a role for MAPK signaling in antitumor drug action, MAPK modulators may have potential as chemotherapeutic drugs themselves or as chemosensitizing agents. The ability of MAPK/ERK kinase (MEK) inhibitors to block survival signaling in specific contexts and promote drug cytotoxicity represents an example, and recent knowledge of the pro-apoptotic functions of **JNK** and p38 suggests possible new approaches to targeted therapy. However, it will be important first to extrapolate the knowledge gained from these laboratory findings, and begin to address the role of MAPKs in the clinical response to chemotherapeutic drugs.

L9 ANSWER 3 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2002089565 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11817656
TITLE: Signalling pathways in cardiac myocyte hypertrophy.
AUTHOR: Sugden P H
CORPORATE SOURCE: National Heart and Lung Institute Division, Faculty of Medicine, Imperial College of Science, Technology and Medicine, London, UK.. p.sugden@ic.ac.uk
SOURCE: Annals of medicine, **(2001 Dec)** 33 (9) 611-22. Ref: 136
Journal code: 8906388. ISSN: 0785-3890.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020131
Last Updated on STN: 20020511
Entered Medline: 20020510

AB In response to a requirement for increased contractile power in vivo, mammalian cardiac myocytes adapt through a hypertrophic response (cell enlargement in the absence of cell division). This response can be simulated by exposing isolated myocytes in primary culture to alpha-adrenergic agonists or the vasoactive peptide, endothelin-1. The signalling pathways responsible for hypertrophic growth have been actively studied, and it is likely that reversible protein phosphorylation and dephosphorylation are involved. Three signalling pathways show particular potential as regulators of the response, ie protein kinase C (PKC), mitogen-activated protein kinase (MAPK) cascades, and calcineurin. These species are thought to regulate the rate and specificity of gene transcription ultimately through modifying the transactivating activity of nuclear transcription factors. There are three pertinent MAPK cascades, the extracellular signal-regulated kinase (ERK) cascade, the c-Jun N-terminal kinase (**JNK** or SAPK1) cascade, and the p38-MAPK (SAPK2-5) cascade. PKC participates in the activation of the ERK cascade but does not contribute significantly to the activation of the two remaining cascades. Calcineurin (or protein phosphatase 2B) is activated by increases in [Ca2+i] through the [Ca2+]-sensing protein, calmodulin. In this **review**, I discuss the evidence for and against the involvement of these signalling proteins in the induction of myocyte hypertrophy and emphasize that the ERK cascade should perhaps feature more widely in the collective consciousness.

L9 ANSWER 4 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2002018598 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11432772
TITLE: Molecular mechanisms of the decision between life and death: regulation of apoptosis by apoptosis signal-regulating kinase 1.
AUTHOR: Matsuzawa A; Ichijo H
CORPORATE SOURCE: Laboratory of Cell Signaling, Graduate School, Tokyo Medical and Dental University, 1-5-45, Yushima, Bunkyo-ku, Tokyo 113-8549, Japan.
SOURCE: Journal of biochemistry, **(2001 Jul)** 130 (1) 1-8. Ref: 65
Journal code: 0376600. ISSN: 0021-924X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20020121
Last Updated on STN: 20020121
Entered Medline: 20011205

AB Coordination and balance between cell survival and apoptosis is crucial for normal development and homeostasis of multicellular organisms. Defects in control of this balance may contribute to a variety of diseases including cancer, autoimmune and neurodegenerative conditions. Although a

large number of pro- and anti-apoptotic factors acting for or against the final death event have been and are being discovered at an extraordinary pace with the recent progress in this area, the molecular mechanisms determining whether a cell lives or dies are not fully understood. Phosphorylation and dephosphorylation of intracellular effector molecules are the most common and important regulatory mechanisms in signal transduction and control a variety of cellular events from cell growth to apoptosis. Apoptosis signal-regulating kinase 1 (ASK1) is a member of the mitogen-activated protein (MAP) kinase kinase kinase family, which activates both the SEK1-**JNK** and MKK3/6-p38 MAP kinase pathways and constitutes a pivotal signaling pathway in cytokine- and stress-induced apoptosis. This **review** provides recent findings on the molecular mechanisms which determine cell fate such as survival, proliferation, differentiation or apoptosis, with special focus on the regulatory mechanisms of ASK1-mediated apoptosis.

L9 ANSWER 5 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2002004617 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11752661
TITLE: Signal integration via PKR.
AUTHOR: Williams B R
CORPORATE SOURCE: The author is in the Department of Cancer Biology, Lerner Research Institute, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195, USA.. williab@ccf.org
SOURCE: Science's STKE [electronic resource] : signal transduction knowledge environment, **(2001 Jul 3)** 2001 (89) RE2. Ref: 69
Journal code: 100964423. ISSN: 1525-8882.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200202
ENTRY DATE: Entered STN: 20020102
Last Updated on STN: 20020212
Entered Medline: 20020211

AB The vital role of interferons (IFNs) as mediators of innate immunity is well established. It has recently become apparent that one of the pivotal proteins in mediating the antiviral activity of IFNs, the double-stranded RNA (dsRNA)-activated protein kinase (PKR), also functions as a signal transducer in the proinflammatory response to different agents. PKR is a member of a small family of kinases that are activated by extracellular stresses and that phosphorylate the alpha subunit of protein synthesis initiation factor eIF-2, thereby inhibiting protein synthesis. The activation of PKR during infection by viral dsRNA intermediates results in the inhibition of viral replication. PKR also mediates the activation of signal transduction pathways by proinflammatory stimuli, including bacterial lipopolysaccharide (LPS), tumor necrosis factor alpha (TNF-alpha), and interleukin 1 (IL-1). PKR is a component of the inhibitor of kappaB (IkappaB) kinase complex and plays either a catalytic or structural role in the activation of IkappaB kinase, depending on the stimulus. The activities of the stress-activated protein kinases p38 and c-Jun NH(2)-terminal kinase (**JNK**) are also regulated by PKR in a pathway that leads to the production of proinflammatory cytokines. This **review** will focus on the role of PKR in nuclear factor kappa B (NF-kappaB) and mitogen-activated protein kinase (MAPK) pathways, because these have been the subjects of a series of publications over the past year that have reported conflicting findings. Although the conflicts may not be resolved in this **review**, suggestions are made for experiments that could lead to a clearer understanding of the mechanisms involved.

L9 ANSWER 6 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2002001591 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11750725
TITLE: Intracellular signaling pathways mediated by the gonadotropin-releasing hormone (GnRH) receptor.
AUTHOR: Kraus S; Naor Z; Seger R
CORPORATE SOURCE: Department of Biological Regulation, The Weizmann Institute of Science, Rehovot, Israel.. sarah.kraus@weizmann.ac.il
SOURCE: Archives of medical research, **(2001 Nov-Dec)** 32 (6) 499-509. Ref: 109
Journal code: 9312706. ISSN: 0188-4409.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20020102
Last Updated on STN: 20020302
Entered Medline: 20020301

AB The hypothalamic gonadotropin-releasing hormone (GnRH) is a key regulator of the reproductive system, triggering the synthesis and release of LH and FSH in the pituitary. GnRH transmits its signal via two specific serpentine receptors that belong to the large group of G-protein coupled receptors (GPCRs). Here we **review** the intracellular signaling pathways mediated by the GnRH receptor (GnRHR). In pituitary-derived alpha T3-1 cells, a widely used model for GnRH action, GnRHR signaling includes activation of mitogen-activated protein kinase (MAPK) cascades, which provide an important link for the transmission of signals from the cell surface to the nucleus and play a role in the regulation of gonadotropin transcription. Activation of ERK--one of the MAPK cascades--by GnRH in these cells depends mainly on the phosphorylation of Raf1 by PKC, supported by a pathway involving c-Src, dynamin, and Ras. On the other hand, the activation of **JNK**, another MAPK cascade, involves PKC, c-Src, CDC42/Rac1, and probably MEKK1. The GnRHR is also expressed in non-pituitary cells and was found to be involved in the inhibition of cell proliferation in certain cells. Therefore, GnRHR represents a potential target for GnRH-analogs used for cancer treatment. Interestingly, the signaling mechanism of the GnRHR in other cell types significantly differs from that in pituitary cells. Studies conducted in GnRHR-expressing COS7 cells have shown that GnRHR transmits its signals mainly via Gi, EGF receptor, c-Src, and is not dependent on PKC. Understanding the signaling mechanisms elicited by GnRHR can shed light on the mechanism of action of GnRH in pituitary and extra-pituitary tissues.

L9 ANSWER 7 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001682444 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11728826
TITLE: The ups and downs of MEK kinase interactions.
AUTHOR: Hagemann C; Blank J L
CORPORATE SOURCE: Department of Cell Physiology and Pharmacology, University of Leicester, Medical Sciences Building, University Road, LE1 9HN, Leicester, UK.
SOURCE: Cellular signalling, **(2001 Dec)** 13 (12) 863-75. Ref: 107
Journal code: 8904683. ISSN: 0898-6568.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011203
Last Updated on STN: 20020420

Entered Medline: 20020110

AB MEK kinases (MEKKs) comprise a family of related serine-threonine protein kinases that regulate mitogen-activated protein kinase (MAPK) signalling pathways leading to c-Jun NH2-terminal kinase (**JNK**) and p38 activation, induced by cellular stress (e.g., UV and gamma irradiation, osmotic stress, heat shock, protein synthesis inhibitors), inflammatory cytokines (e.g., tumour necrosis factor alpha, TNFalpha, and interleukin-1, IL1) and G protein-coupled receptor agonists (e.g., thrombin). These stress-activated kinases have been implicated in apoptosis, oncogenic transformation, and inflammatory responses in various cell types. At present, the signalling events involving MEKKs are not well understood. This **review** summarises our current knowledge concerning the regulation and function of MEKK family members, with particular emphasis on those factors capable of directly interacting with distinct MEKK isoforms.

L9 ANSWER 8 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001640850 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11692153
TITLE: Recent advances in molecular genetics of breast cancer.
AUTHOR: Pavelic K; Gall-Troselj K
CORPORATE SOURCE: Ruder Boskovic Institute, Division of Molecular Medicine, Bijenicka 54, P.O. Box 180, 10002 Zagreb, Croatia.. pavelic@rudjer.irb.hr
SOURCE: Journal of molecular medicine (Berlin, Germany), **(2001 Oct)** 79 (10) 566-73. Ref: 58
Journal code: 9504370. ISSN: 0946-2716.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011107
Last Updated on STN: 20020123
Entered Medline: 20011219

AB Breast cancer is among the most common tumors affecting women. It is characterized by a number of genetic aberrations. Some 5-10% of cases are thought to be inherited. The hereditary breast and ovarian cancer syndrome includes genetic alterations of various susceptibility genes, particularly BRCA1 and BRCA2. Breast tumors of patients with germ-line mutations in the BRCA1 and BRCA2 genes have more genetic defects than sporadic breast tumors. Here we **review** new findings in the function of BRCA1 gene function. Accumulation of somatic genetic changes during tumor progression map follows a specific and more aggressive pathway of chromosome damage in these individuals. A major BRCA1 downstream target gene is the DNA damage-responsive gene GADD45. Induction of BRCA1 triggers apoptosis by activation of c-Jun N-terminal kinase/stress-activated protein kinase (**JNK**/SAPK). BRCA1 interacts with SWI/SNF, a chromatin remodeling complex important in gene expression. Recent advances in genomics and bioinformatics, particularly in DNA-sequencing approaches and DNA-chip technology are expected to improve identification of small molecules, which might be drugable targets. New knowledge about the genetic portrait of breast tumor is coming from differential gene expression profiling using microarrays. Human genome studies, as well as development of "DNA chips," provide a window for observing patterns of gene activity in cells, which will contribute to more accurate cancer classification. However, substantial work connected with analytical and statistical tools must still be carried out to confirm the function of differentially expressed genes. Knowledge of the molecular characteristics of breast tumor has already started to make possible the identification of breast cancer patients who could benefit from therapies that target those features. Progress in basic research into signaling provides the opportunity to attack at least some signal-transduction targets involved in proliferation, survival, invasion, angiogenesis, metastasis, and resistance. Exciting knowledge in breast cancer biology is rapidly accumulating in parallel with recent developments in rational selection and validation of relevant targets that provide unique opportunities for development of "intelligent" therapeutics.

L9 ANSWER 9 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001568186 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11675147
TITLE: Genotoxic and non-genotoxic pathways of p53 induction.
AUTHOR: Pluquet O; Hainaut P
CORPORATE SOURCE: Group of Molecular Carcinogenesis, International Agency for Research on Cancer, 150 Cours Albert Thomas, 69372, Lyon, France.
SOURCE: Cancer letters, **(2001 Dec 10)** 174 (1) 1-15. Ref: 132
Journal code: 7600053. ISSN: 0304-3835.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011025
Last Updated on STN: 20020122
Entered Medline: 20011212

AB Since the initial concept of p53 as a sensor of DNA-damage, the picture of the role of p53 has widened to include the sensing of much more diverse forms of stress, including hypoxia and constitutive activation of growth-promoting cascades. The pathways by which these processes regulate p53 are partially overlapping, but imply different patterns of post-translational modifications. In this **review**, we summarize current knowledge on post-translational modifications of p53, and we discuss how hypoxia and oncogene activation stresses may induce p53 independently of DNA damage.

L9 ANSWER 10 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001523369 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11570006
TITLE: [Molecular regulation of myocardial apoptosis].
A szivizom apoptosisanak molekularis szabalyozasa.
AUTHOR: Andreka P; Nadhazi Z; Muzes G; Bishopric N H
CORPORATE SOURCE: Altalanos Orvostudomanyi Kar, II. Belgyogyaszati Klinika, Semmelweis Egyetem, Budapest.
SOURCE: Orvosi hetilap, **(2001 Aug 12)** 142 (32) 1717-24.
Ref: 50
Journal code: 0376412. ISSN: 0030-6002.
PUB. COUNTRY: Hungary
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Hungarian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200203
ENTRY DATE: Entered STN: 20010926
Last Updated on STN: 20020315
Entered Medline: 20020314

AB Since apoptosis was described as a process distinct from necrosis, there have been many studies of programmed cell death in diseases, especially immunological diseases. Because cardiac myocytes are terminally differentiated cells, they have typically been assumed to die exclusively by necrosis. However, during the last six to seven years this view has been challenged by several studies demonstrating that a significant number

of myocytes undergo apoptosis in myocardial infarction, heart failure, myocarditis, arrhythmogen right ventricular dysplasia, and immune rejection after cardiac transplantation, as well as in other conditions of stress. These are potentially very important observations, because apoptosis--unlike necrosis--can be blocked or reversed at early stages. The tracking of cytoprotective and apoptotic signal transduction pathways has proceeded rapidly with important new insights into the roles of mitochondria-dependent pathway, Bcl-2 protein family, p38 mitogen-activated protein kinase, extracellular signal-regulated kinase and c-Jun N-terminal kinase in cell fate. New studies have demonstrated that specific inhibition of apoptosis and activation of cytoprotective mechanisms, based on the better understanding of the intracellular signaling pathways, can significantly protect cardiac myocytes. This **review** will assess progress in cardiac myocyte apoptosis research and report on the current status of anti-apoptotic therapy in acute and chronic heart diseases.

L9 ANSWER 11 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001460639 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11506194
TITLE: Signaling by the **JNK** group of MAP kinases. c-jun N-terminal Kinase.
AUTHOR: Dong C; Davis R J; Flavell R A
CORPORATE SOURCE: Section of Immunobiology, Yale University School of Medicine and Howard Hughes, Medical Institute, New Haven, Connecticut 06520, USA.
SOURCE: Journal of clinical immunology, **(2001 Jul)** 21 (4) 253-7. Ref: 30
Journal code: 8102137. ISSN: 0271-9142.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20020201
Entered Medline: 20020131

AB c-Jun N-terminal kinase (**JNK**) is one of the several main MAP kinase groups identified in mammals. Original studies by use of Jurkat T cells implicated **JNK** in T cell activation and interleukin (IL-2) expression. Recent advances using mouse genetic approaches have revealed novel functions of this pathway in primary mouse T cells. **JNK** is not essential for T-cell activation; instead, it is required for helper T differentiation into effector cells and their cytokine production. In this **review**, we summarize these advances in understanding the expression, function, and regulation of the **JNK** pathway in T-lymphocyte activation and differentiation.

L9 ANSWER 12 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001424827 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11472310
TITLE: Mitogen-activated protein kinase signal transduction in skeletal muscle: effects of exercise and muscle contraction.
AUTHOR: Widegren U; Ryder J W; Zierath J R
CORPORATE SOURCE: Department of Clinical Physiology, Karolinska Hospital, Stockholm, Sweden.
SOURCE: Acta physiologica Scandinavica, **(2001 Jul)** 172 (3) 227-38. Ref: 101
Journal code: 0370362. ISSN: 0001-6772.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011008
Last Updated on STN: 20011008
Entered Medline: 20011004

AB Exercise has numerous growth and metabolic effects in skeletal muscle, including changes in glycogen metabolism, glucose and amino acid uptake, protein synthesis and gene transcription. However, the mechanism(s) by which exercise regulates intracellular signal transduction to the transcriptional machinery in the nucleus, thus modulating gene expression, is largely unknown. This **review** will provide insight on potential intracellular signalling mechanisms by which muscle contraction/exercise leads to changes in gene expression. Mitogen-activated protein kinase (MAPK) cascades are associated with increased transcriptional activity. The MAPK family members can be separated into distinct parallel pathways including the extracellular signal-regulated kinase (ERK) 1/2, the stress-activated protein kinase cascades (SAPK1/**JNK** and SAPK2/p38) and the extracellular signal-regulated kinase 5 (ERK5). Acute exercise elicits signal transduction via MAPK cascades in direct response to muscle contraction. Thus, MAPK pathways appear to be potential physiological mechanisms involved in the exercise-induced regulation of gene expression in skeletal muscle.

L9 ANSWER 13 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001345749 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11408795
TITLE: The role of Epstein-Barr virus in neoplastic transformation.
AUTHOR: Knecht H; Berger C; Rothenberger S; Odermatt B F; Brousset P
CORPORATE SOURCE: Institute for Clinical Research, Swiss Paraplegic Centre, Nottwil, Switzerland.. hans.knecht@paranet.ch
SOURCE: Oncology, **(2001)** 60 (4) 289-302. Ref: 148
Journal code: 0135054. ISSN: 0030-2414.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010730
Last Updated on STN: 20010730
Entered Medline: 20010726

AB In this **review**, we focus on new data from basic, translational and clinical research relating to the Epstein-Barr virus (EBV). Beside its well-known tropism for B lymphocytes and epithelial cells, EBV also infects T lymphocytes, monocytes and granulocytes. After primary infection, EBV persists throughout the life span in resting memory B cells, from where it is reactivated upon breakdown of cellular immunity. In the process of neoplastic transformation, the EBV-encoded latent membrane protein 1 (LMP1) oncogene represents the major driving force. LMP1 acts like a constitutively activated receptor of the tumor necrosis factor receptor family and allows the amplification or bypassing of physiological regulatory signals through direct and indirect interactions with proteins of the tumor necrosis factor receptor-associated factor (TRAF) family. TRAF2-mediated NF-kappaB activation, AP-1 induction and JAK3/STAT activation may result in sustained proliferation leading to lymphoma. The ability of LMP1 to suppress germinal center formation and its capacity to mediate its own transcriptional activation shed new light on the pathogenesis of EBV-associated latency type II lymphoproliferations like Hodgkin's disease and angioimmunoblastic lymphadenopathy. The

carboxy terminus of LMP1 is also a reliable marker for individual EBV strain identification and thus offers new possibilities in tracing the molecular events leading to posttransplant lymphoproliferative disorders (PTLDs). Cytotoxic T lymphocytes directed against well-characterized epitopes of EBV latency genes represent an already successful and promising therapeutic approach to EBV-associated lymphomas, in particular PTLDs.

L9 ANSWER 14 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001344156 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11407210
TITLE: The bronchial epithelium in asthma--much more than a passive barrier.
AUTHOR: Hamilton L M; Davies D E; Wilson S J; Kimber I; Dearman R J; Holgate S T
CORPORATE SOURCE: Respiratory, Cell and Molecular Biology Division, School of Medicine, University of Southampton, Southampton General Hospital, Tremona Road, Southampton, SO16 6YD.
SOURCE: Monaldi archives for chest disease = Archivio Monaldi per le malattie del torace / Fondazione clinica del lavoro, IRCCS [and] Istituto di clinica tisiologica e malattie apparato respiratorio, Universita di Napoli, Secondo ateneo, **(2001 Feb)** 56 (1) 48-54. Ref: 43
Journal code: 9307314. ISSN: 1122-0643.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010827
Last Updated on STN: 20010827
Entered Medline: 20010823

AB The bronchial epithelium has a multifunctional role in the airway. It is actively engaged in communicating with cells of the immune and inflammatory systems, as well as secreting cytoprotective molecules and acting as a physical barrier between the internal and external milieu of the lungs. In asthma, the bronchial epithelium is often damaged, with shedding of the columnar cells into the airway lumen. This damage and ensuing repair responses are proposed to orchestrate airway remodelling via activation of myofibroblasts in the underlying lamina reticularis. This allows the two cell types to work as a trophic unit, propagating and amplifying the response at the cell surface into the submucosa. In addition to structural damage, the epithelium displays an "activated" phenotype evident by activation of transcription factors such as nuclear factor kappa B (NF kappa B), and expression of mediators which directly or indirectly lead to a chronic cycle of inflammation and injury. A diverse number of innocuous stimuli trigger asthma. It is likely that interactions between genetic and environmental factors converge on common intracellular signalling pathways that regulate epithelial stress and repair. Of particular relevance is the NF kappa B signalling pathway and the mitogen activated protein kinase pathways (MAPKs), of which the mitogen activated extracellular regulated kinases (ERKs), and the stress activated P38 and c-Jun NH2 terminal kinase (**JNKs**) are best known. This **review** aims to highlight the importance of these signalling pathways in coordinating the response to diverse stimuli at the surface of the bronchial epithelium which leads to development and maintenance of the asthmatic state.

L9 ANSWER 15 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001337848 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11167129
TITLE: Tumor necrosis factor receptor-associated factor (TRAF) 2 and its role in TNF signaling.
AUTHOR: Wajant H; Scheurich P
CORPORATE SOURCE: Institute of Cell Biology and Immunology, University of Stuttgart, Allmandring 31, Stuttgart 70569, Germany.. harald.wajant@po.uni-stuttgart.de
SOURCE: international journal of biochemistry & cell biology, **(2001 Jan)** 33 (1) 19-32. Ref: 104
Journal code: 9508482. ISSN: 1357-2725.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010618
Last Updated on STN: 20010618
Entered Medline: 20010614

AB Tumor necrosis factor (TNF) is the prototypic member of the TNF ligand family and has a key role in the regulation of inflammatory processes. TNF exerts its functions by interaction with the death domain-containing TNF-receptor 1 (TNF-R1) and the non-death domain-containing TNF-receptor 2 (TNF-R2), both members of a receptor family complementary to the TNF ligand family. Due to the prototypic features of the TNF receptors and their importance for the regulation of inflammation, the signal transduction mechanisms utilized by these receptors have been extensively studied. Several proteins that interact directly or indirectly with the cytoplasmic domains of TNF-R1 and TNF-R2 have been identified in the recent years giving ideas how these receptors are connected to the apoptotic pathway and the signaling cascades leading to activation of NF-kappaB and **JNK**. Of special interest are TNF receptor-associated factor (TRAF) 1 and 2, which defines a novel group of adaptor proteins involved in signal transduction by most members of the TNF receptor family, of IL-1 receptor and IL-17 receptor as well as some members of the TOLL-like receptor family. TRAF 2 is currently the best-characterized TRAF family member, having a key role in mediating TNF-R1-induced activation of NF-kappaB and **JNK**. Moreover, recent studies suggest that TRAF 2 represents an integration point for pro- and antiapoptotic signals. This **review** focuses on the molecular mechanisms that underlay signal initiation by TNF-R1 and TNF-R2, with particular consideration of the role of TRAF 2, and highlights the importance of this molecule for the integration of such antagonizing pathways as death induction and NF-kappaB-mediated surviving signals.

L9 ANSWER 16 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001332709 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11402338
TITLE: AP-1 proteins in the adult brain: facts and fiction about effectors of neuroprotection and neurodegeneration.
AUTHOR: Herdegen T; Waetzig V
CORPORATE SOURCE: Institute of Pharmacology, Hospitalstrasse 4, 24105 Kiel, Germany.
SOURCE: Oncogene, **(2001 Apr 30)** 20 (19) 2424-37. Ref: 136
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705

AB Jun and Fos proteins are induced and activated following most physiological and pathophysiological stimuli in the brain. Only few data allow conclusions about distinct functions of AP-1 proteins in neurodegeneration and neuroregeneration, and these functions mainly refer to c-Jun and its activation by **JNKs**. Apoptotic functions of activated c-Jun affect hippocampal, nigral and primary cultured neurons following excitotoxic stimulation and destruction of the neuron-target-axis including withdrawal of trophic molecules. The inhibition of **JNKs** might exert neuroprotection by subsequent omission of c-Jun activation. Besides endogenous neuronal functions, the c-Jun/AP-1 proteins can damage the nervous system by upregulation of harmful programs in non-neuronal cells (e.g. microglia) with release of neurodegenerative molecules. In contrast, the differentiation with neurite extension and maturation of neural cells in vitro indicate physiological and potentially neuroprotective functions of c-Jun and **JNKs** including sensoring for alterations in the cytoskeleton. This **review** summarizes the multiple molecular interfunctions which are involved in the shift from the physiological role to degenerative effects of the Jun/**JNK**-axis such as cell type-specific expression and intracellular localization of scaffold proteins and upstream activators, antagonistic phosphatases, interaction with other kinase systems, or the activation of transcription factors competing for binding to **JNK** proteins and AP-1 DNA elements.

L9 ANSWER 17 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001332703 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11402332
TITLE: Drosophila AP-1: lessons from an invertebrate.
AUTHOR: Kockel L; Homsy J G; Bohmann D
CORPORATE SOURCE: Department of Genetics, Harvard Medical School, 200 Longwood Avenue, Boston, Massachusetts, MA 02115, USA.
SOURCE: Oncogene, **(2001 Apr 30)** 20 (19) 2347-64. Ref: 112
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200107
ENTRY DATE: Entered STN: 20010709
Last Updated on STN: 20010709
Entered Medline: 20010705

AB In recent years, studies in the model organism Drosophila melanogaster have contributed significant insights into the molecular and developmental biology of the AP-1 transcription factors Jun and Fos. Powerful genetic and biochemical approaches uncovered a baffling complexity and variability of the signaling connections to and from AP-1. The range of biological processes that Jun and Fos regulate in this organism is equally multi-faceted. Regulatory interactions between AP-1 and **JNK**, ERK, TGFbeta, Notch or other signaling systems have been implicated in the control of a multitude of embryonic and adult events, including tissue closure processes, patterning of eye, gut and wing, as well as apoptosis. Here we **review** the information that has been gathered on Drosophila AP-1 in signal transduction and on the developmental and cellular functions controlled by AP-1-mediated signals in the fly. Lessons learned from the studies on AP-1 in Drosophila may contribute to our general understanding, beyond species boundaries, of this fundamental class of transcriptional regulators.

L9 ANSWER 18 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001297573 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11378302
TITLE: Mitogen-activated protein kinase signalling in oligodendrocytes: a comparison of primary cultures and CG-4.
AUTHOR: Stariha R L; Kim S U
CORPORATE SOURCE: Department of Medicine, Division of Neurology, UBC Hospital, University of British Columbia, 2211 Wesbrook Mall, BC, V6T 2B5, Vancouver, Canada.
SOURCE: International journal of developmental neuroscience : official journal of the International Society for Developmental Neuroscience, **(2001 Jul)** 19 (4) 427-37.
Journal code: 8401784. ISSN: 0736-5748.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20010813
Entered Medline: 20010809

AB Oligodendrocytes play a significant role in the central nervous system, as these cells are responsible for myelinating axons and allowing for the efficient conduction of nerve impulses. Therefore, any understanding we can gain about the functional biology of oligodendrocytes will give us important insights into demyelinating diseases such as multiple sclerosis, where oligodendrocytes and myelin are damaged or destroyed. Currently, much attention has focussed on the role of a family of mitogen-activated protein kinases in OL. This kinase family includes the extracellular signal-regulated protein kinases (ERKs), the stress-activated c-Jun N-terminal kinase (**JNK**), and the 38 kDa high osmolarity glycerol response kinase (p38). The actions of mitogen-activated protein kinases in oligodendrocytes appear to range from proliferation and cell survival to differentiation and cell death. In the past, studies on oligodendrocytes have been hampered by the difficulties inherent in producing large enough quantities of these cells for experimentation. This problem arises in large part due to the post-mitotic nature of mature oligodendrocytes. Over the years, a cell line known as Central Glia-4 (CG-4) has become a popular oligodendrocyte model due to its potentially unlimited capacity for self-renewal. In this **review**, we will look at the suitability of the Central Glia-4 cell line as an oligodendrocyte model, specifically in respect to studies on mitogen-activated protein kinase signalling in oligodendrocytes.

L9 ANSWER 19 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001276847 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11369511
TITLE: Signalling for survival and death in neurones: the role of stress-activated kinases, **JNK** and p38.
AUTHOR: Harper S J; LoGrasso P
CORPORATE SOURCE: Department of Pharmacology, Merck Sharp and Dohme Research Laboratories, Neuroscience Research Centre, Terlings Park, Essex CM20 2QR, Harlow, UK.. sarah_harper@merck.com
SOURCE: Cellular signalling, **(2001 May)** 13 (5) 299-310. Ref: 150
Journal code: 8904683. ISSN: 0898-6568.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20010813
Entered Medline: 20010809

AB The pathways involved in neuronal survival or death have been extensively

studied mainly in cell lines. Recent evidence has suggested that activation of the stress activated pathways, jun N-terminal kinase (**JNK**) and p38 may play important roles in neuronal cell death or regeneration. In this **review** we will discuss these pahtways in detail. We will examine the evidence that these pathways are important in neuronal cell death. Finally we will **review** the evidence that inhibitors of these pathways have a neuroprotective effect both in vitro and in vivo.

L9 ANSWER 20 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001261567 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11302723
TITLE: Nitric oxide as a bioregulator of apoptosis.
AUTHOR: Chung H T; Pae H O; Choi B M; Billiar T R; Kim Y M
CORPORATE SOURCE: Department of Microbiology and Immunology, Wonkwang University, Chunbug, 570-749, Korea.. htchung@wonnms.wonkwang.ac.kr
SOURCE: Biochemical and biophysical research communications, **(2001 Apr 20)** 282 (5) 1075-9. Ref: 52
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010521
Last Updated on STN: 20010521
Entered Medline: 20010517

AB Nitric oxide (NO), synthesized from l-arginine by NO synthases, is a small, diffusible, highly reactive molecule with dichotomous regulatory roles under physiological and pathological conditions. NO can promote apoptosis (proapoptosis) in some cells, whereas it inhibits apoptosis (antiapoptosis) in other cells. This complexity is a consequence of the rate of NO production and the interaction with biological molecules such as iron, thiols, proteins, and reactive oxygen species. Long-lasting production of NO acts as a proapoptotic modulator by activating caspase family proteases through the release of mitochondrial cytochrome c into the cytosol, upregulation of p53 expression, activation of **JNK** /SAPK, and altering the expression of apoptosis-associated proteins including Bcl-2 family proteins. However, low or physiological concentrations of NO prevent cells from apoptosis induced by trophic factor withdrawal, Fas, TNFalpha, and lipopolysaccharide. The antiapoptotic mechanism can be understood via expression of protective genes such as heat shock proteins, Bcl-2 as well as direct inhibition of the apoptotic caspase family proteases by S-nitrosylation of the cysteine thiol. Our current understanding of the mechanisms by which NO exerts both pro- and antiapoptotic actions is discussed in this **review** article.

L9 ANSWER 21 OF 21 MEDLINE on STN
ACCESSION NUMBER: 2001108089 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11145972
TITLE: The neuronal MAP kinase cascade: a biochemical signal integration system subserving synaptic plasticity and memory.
AUTHOR: Sweatt J D
CORPORATE SOURCE: Division of Neuroscience, Baylor College of Medicine, Houston, Texas 77030-3498, USA.. jsweatt@bcm.tmc.edu
SOURCE: Journal of neurochemistry, **(2001 Jan)** 76 (1) 1-10. Ref: 65
Journal code: 2985190R. ISSN: 0022-3042.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010208

AB The mitogen-activated protein kinase (MAP kinase, MAPK) cascade, as the name implies, was originally discovered as a critical regulator of cell division and differentiation. As further details of this signaling cascade were worked out, it became clear that the MAPK cascade is in fact a prototype for a family of signaling cascades that share the motif of three serially linked kinases regulating each other by sequential phosphorylation. Thus, a revised nomenclature arose that uses the term MAPK to refer to the entire superfamily of signaling cascades (comprising the erks, the **JNKs** and the p38 stress activated protein kinases), and specifies the prototype MAPK as the extracellular signal-regulated kinase (erk). The two erk MAPK isoforms, p44 MAPK and p42 MAPK, are referred to as erk1 and erk2, respectively.The erks are abundantly expressed in neurons in the mature central nervous system, raising the question of why the prototype molecular regulators of cell division and differentiation are present in these non-dividing, terminally differentiated neurons. This **review** will describe the beginnings of an answer to this question. Interestingly, the general model has begun to emerge that the erk signaling system has been co-opted in mature neurons to function in synaptic plasticity and memory. Moreover, recent insights have led to the intriguing prospect that these molecules serve as biochemical signal integrators and molecular coincidence detectors for coordinating responses to extracellular signals in neurons. In this **review** I will first outline the essential components of this signal transduction cascade, and briefly describe recent results implicating the erks in mammalian synaptic plasticity and learning. I will then proceed to outline recent results implicating the erks as molecular signal integrators and, potentially, coincidence detectors. Finally, I will speculate on what the critical downstream effectors of the erks are in neurons, and how they might provide a readout of the integrated signal.

=> LOG HOLD

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	11.46	179.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.40

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STN INTERNATIONAL SESSION SUSPENDED AT 07:37:16 ON 02 DEC 2004

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LOGINID:sssptal623zct

PASSWORD:
* * * * * * RECONNECTED TO STN INTERNATIONAL * * * * * *
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FILE 'MEDLINE' ENTERED AT 08:00:15 ON 02 DEC 2004

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FULL ESTIMATED COST                                11.46     179.85

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
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=> D HIS

     (FILE 'HOME' ENTERED AT 07:19:11 ON 02 DEC 2004)

     FILE 'REGISTRY' ENTERED AT 07:19:14 ON 02 DEC 2004
L1              STRUCTURE UPLOADED
L2           16 S L1

     FILE 'CAPLUS' ENTERED AT 07:19:37 ON 02 DEC 2004
L3            1 S L2

     FILE 'REGISTRY' ENTERED AT 07:20:08 ON 02 DEC 2004
L4          307 S L1 SSS FULL

     FILE 'CAPLUS' ENTERED AT 07:20:19 ON 02 DEC 2004
L5            3 S L4
L6            2 S L5 NOT L3

     FILE 'MEDLINE' ENTERED AT 07:26:37 ON 02 DEC 2004
L7         6059 S JNK
L8          132 S L7 AND REVIEW
L9           21 S L8 AND 2001/PY

=> S L7 AND DEFICIENCY
        201718 DEFICIENCY
         19531 DEFICIENCIES
        214611 DEFICIENCY
                (DEFICIENCY OR DEFICIENCIES)
L10        221 L7 AND DEFICIENCY

=> S L10 AND 2001/PY
        516039 2001/PY
L11         27 L10 AND 2001/PY

=> D 27

L11  ANSWER 27 OF 27     MEDLINE on STN
AN   2001180181     MEDLINE
DN   PubMed ID: 11157857
TI   Decreased immediate inflammatory gene induction in activating
     transcription factor-2 mutant mice.
AU   Reimold A M; Kim J; Finberg R; Glimcher L H
CS   Rheumatic Diseases Division, University of Texas Southwestern Medical
     Center, Dallas, TX 75390-8884, USA.
NC   AI 3241200 (NIAID)
SO   International immunology, (2001 Feb) 13 (2) 241-8.
     Journal code: 8916182. ISSN: 0953-8178.
CY   England: United Kingdom
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200105
ED   Entered STN: 20010517
     Last Updated on STN: 20021015
     Entered Medline: 20010503

=> S JNK DEFICIENCY
          5977 JNK
           436 JNKS
          6059 JNK
                (JNK OR JNKS)
        201718 DEFICIENCY
         19531 DEFICIENCIES
        214611 DEFICIENCY
                (DEFICIENCY OR DEFICIENCIES)
L12          2 JNK DEFICIENCY
                (JNK(W)DEFICIENCY)

=> D 1-2

L12  ANSWER 1 OF 2     MEDLINE on STN
AN   2003115527     MEDLINE
DN   PubMed ID: 12629045
TI   Suppression of Ras-stimulated transformation by the JNK signal
     transduction pathway.
AU   Kennedy Norman J; Sluss Hayla K; Jones Stephen N; Bar-Sagi Dafna; Flavell
     Richard A; Davis Roger J
CS   Howard Hughes Medical Institute, University of Massachusetts Medical
     School, Worcester, Massachusetts 01605, USA.
SO   Genes & development, (2003 Mar 1) 17 (5) 629-37.
     Journal code: 8711660. ISSN: 0890-9369.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200304
ED   Entered STN: 20030312
     Last Updated on STN: 20030417
     Entered Medline: 20030415

L12  ANSWER 2 OF 2     MEDLINE on STN
AN   2001519675     MEDLINE
DN   PubMed ID: 11566876
TI   jkk-1 and mek-1 regulate body movement coordination and response to heavy
     metals through jnk-1 in Caenorhabditis elegans.
AU   Villanueva A; Lozano J; Morales A; Lin X; Deng X; Hengartner M O;
     Kolesnick R N
CS   Laboratory of Signal Transduction, Memorial Sloan-Kettering Cancer Center,
     New York, NY 10021, USA.
NC   CA-42385 (NCI)
     GM-52540 (NIGMS)
SO   EMBO journal, (2001 Sep 17) 20 (18) 5114-28.
     Journal code: 8208664. ISSN: 0261-4189.
CY   England: United Kingdom
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
OS   GENBANK-AB024085
EM   200110
ED   Entered STN: 20010924
     Last Updated on STN: 20011029
     Entered Medline: 20011025

=> D ABS 1

L12  ANSWER 1 OF 2     MEDLINE on STN
AB   The c-Jun NH(2)-terminal kinase (JNK) phosphorylates and activates members
     of the activator protein-1 (AP-1) group of transcription factors and is
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implicated in oncogenic transformation. To examine the role of JNK, we investigated the effect of **JNK deficiency** on Ras-stimulated transformation. We demonstrate that although JNK does play a role in transformation in vitro, JNK is not required for tumor development in vivo. Importantly, the loss of JNK expression resulted in substantial increases in the number and growth of tumor nodules in vivo. Complementation assays demonstrated that this phenotype was caused by **JNK deficiency.** These data demonstrate that, in contrast to expectations, the normal function of JNK may be to suppress tumor development in vivo. This conclusion is consistent with the presence in human tumors of loss-of-function mutations in the JNK pathway.

JNK DEFICIENCY
↑ TUMOR

=> LOGOFF
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	13.54	181.93

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.40

STN INTERNATIONAL LOGOFF AT 08:02:40 ON 02 DEC 2004